SEQUENCE LISTING

<110>   F. Hoffmann-La Roche AG

<120>   Method for the recombinant expression of an N-terminal fragment
        of hepatocyte growth factor

<130>   22388 WO

<150>   EP 04004951.2
<151>   2004-03-03

<160>   4

<170>   PatentIn version 3.2

<210>   1
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<212>   DNA
<213>   Homo sapiens


<220>
<221>   CDS
<222>   (1)..(1389)
<223>   DNA sequence encoding the alpha-chain of hepatocyte growth factor
        (HGF)


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caa agg aaa aga aga aat aca att cat gaa ttc aaa aaa tca gca aag        48
Gln Arg Lys Arg Arg Asn Thr Ile His Glu Phe Lys Lys Ser Ala Lys
1               5               10                  15

act acc cta atc aaa ata gat cca gca ctg aag ata aaa acc aaa aaa        96
Thr Thr Leu Ile Lys Ile Asp Pro Ala Leu Lys Ile Lys Thr Lys Lys
                20                  25                  30

gtg aat act gca gac caa tgt gct aat aga tgt act agg aat aaa gga       144
Val Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn Lys Gly
            35                  40                  45

ctt cca ttc act tgc aag gct ttt gtt ttt gat aaa gca aga aaa caa       192
Leu Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg Lys Gln
        50                  55                  60

tgc ctc tgg ttc ccc ttc aat agc atg tca agt gga gtg aaa aaa gaa       240
Cys Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys Lys Glu
65                  70                  75                  80

ttt ggc cat gaa ttt gac ctc tat gaa aac aaa gac tac att aga aac       288
Phe Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile Arg Asn
                85                  90                  95
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tgc atc att ggt aaa gga cgc agc tac aag gga aca gta tct atc act        336
Cys Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser Ile Thr
            100                 105                 110

aag agt ggc atc aaa tgt cag ccc tgg agt tcc atg ata cca cac gaa        384
Lys Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro His Glu
            115                 120                 125

cac agc ttt ttg cct tcg agc tat cgg ggt aaa gac cta cag gaa aac        432
His Ser Phe Leu Pro Ser Ser Tyr Arg Gly Lys Asp Leu Gln Glu Asn
            130                 135                 140

tac tgt cga aat cct cga ggg gaa gaa ggg gga ccc tgg tgt ttc aca        480
Tyr Cys Arg Asn Pro Arg Gly Glu Glu Gly Gly Pro Trp Cys Phe Thr
145                 150                 155                 160

agc aat cca gag gta cgc tac gaa gtc tgt gac att cct cag tgt tca        528
Ser Asn Pro Glu Val Arg Tyr Glu Val Cys Asp Ile Pro Gln Cys Ser
                165                 170                 175

gaa gtt gaa tgc atg acc tgc aat ggg gag agt tat cga ggt ctc atg        576
Glu Val Glu Cys Met Thr Cys Asn Gly Glu Ser Tyr Arg Gly Leu Met
            180                 185                 190

gat cat aca gaa tca ggc aag att tgt cag cgc tgg gat cat cag aca        624
Asp His Thr Glu Ser Gly Lys Ile Cys Gln Arg Trp Asp His Gln Thr
            195                 200                 205

cca cac cgg cac aaa ttc ttg cct gaa aga tat ccc gac aag ggc ttt        672
Pro His Arg His Lys Phe Leu Pro Glu Arg Tyr Pro Asp Lys Gly Phe
            210                 215                 220

gat gat aat tat tgc cgc aat ccc gat ggc cag ccg agg cca tgg tgc        720
Asp Asp Asn Tyr Cys Arg Asn Pro Asp Gly Gln Pro Arg Pro Trp Cys
225                 230                 235                 240

tat act ctt gac cct cac acc cgc tgg gag tac tgt gca att aaa aca        768
Tyr Thr Leu Asp Pro His Thr Arg Trp Glu Tyr Cys Ala Ile Lys Thr
                245                 250                 255

tgc gct gac aat act atg aat gac act gat gtt cct ttg gaa aca act        816
Cys Ala Asp Asn Thr Met Asn Asp Thr Asp Val Pro Leu Glu Thr Thr
            260                 265                 270

gaa tgc atc caa ggt caa gga gaa ggc tac agg ggc act gtc aat acc        864
Glu Cys Ile Gln Gly Gln Gly Glu Gly Tyr Arg Gly Thr Val Asn Thr
            275                 280                 285

att tgg aat gga att cca tgt cag cgt tgg gat tct cag tat cct cac        912
Ile Trp Asn Gly Ile Pro Cys Gln Arg Trp Asp Ser Gln Tyr Pro His
            290                 295                 300

gag cat gac atg act cct gaa aat ttc aag tgc aag gac cta cga gaa        960
Glu His Asp Met Thr Pro Glu Asn Phe Lys Cys Lys Asp Leu Arg Glu
305                 310                 315                 320
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aat tac tgc cga aat cca gat ggg tct gaa tca ccc tgg tgt ttt acc    1008
Asn Tyr Cys Arg Asn Pro Asp Gly Ser Glu Ser Pro Trp Cys Phe Thr
            325             330                     335

act gat cca aac atc cga gtt ggc tac tgc tcc caa att cca aac tgt    1056
Thr Asp Pro Asn Ile Arg Val Gly Tyr Cys Ser Gln Ile Pro Asn Cys
            340             345                 350

gat atg tca cat gga caa gat tgt tat cgt ggg aat ggc aaa aat tat    1104
Asp Met Ser His Gly Gln Asp Cys Tyr Arg Gly Asn Gly Lys Asn Tyr
            355             360                 365

atg ggc aac tta tcc caa aca aga tct gga cta aca tgt tca atg tgg    1152
Met Gly Asn Leu Ser Gln Thr Arg Ser Gly Leu Thr Cys Ser Met Trp
        370             375             380

gac aag aac atg gaa gac tta cat cgt cat atc ttc tgg gaa cca gat    1200
Asp Lys Asn Met Glu Asp Leu His Arg His Ile Phe Trp Glu Pro Asp
385             390             395             400

gca agt aag ctg aat gag aat tac tgc cga aat cca gat gat gat gct    1248
Ala Ser Lys Leu Asn Glu Asn Tyr Cys Arg Asn Pro Asp Asp Asp Ala
            405             410             415

cat gga ccc tgg tgc tac acg gga aat cca ctc att cct tgg gat tat    1296
His Gly Pro Trp Cys Tyr Thr Gly Asn Pro Leu Ile Pro Trp Asp Tyr
            420             425             430

tgc cct att tct cgt tgt gaa ggt gat acc aca cct aca ata gtc aat    1344
Cys Pro Ile Ser Arg Cys Glu Gly Asp Thr Thr Pro Thr Ile Val Asn
            435             440             445

tta gac cat ccc gta ata tct tgt gcc aaa acg aaa caa ttg cga        1389
Leu Asp His Pro Val Ile Ser Cys Ala Lys Thr Lys Gln Leu Arg
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Gln Arg Lys Arg Arg Asn Thr Ile His Glu Phe Lys Lys Ser Ala Lys
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Thr Thr Leu Ile Lys Ile Asp Pro Ala Leu Lys Ile Lys Thr Lys Lys
            20                  25                  30


Val Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn Lys Gly
            35                  40                  45


Leu Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg Lys Gln
        50                  55                  60
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Cys Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys Lys Glu
65              70              75                  80

Phe Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile Arg Asn
                85              90                  95

Cys Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser Ile Thr
            100             105             110

Lys Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro His Glu
        115             120             125

His Ser Phe Leu Pro Ser Ser Tyr Arg Gly Lys Asp Leu Gln Glu Asn
    130             135             140

Tyr Cys Arg Asn Pro Arg Gly Glu Glu Gly Gly Pro Trp Cys Phe Thr
145             150             155             160

Ser Asn Pro Glu Val Arg Tyr Glu Val Cys Asp Ile Pro Gln Cys Ser
            165             170             175

Glu Val Glu Cys Met Thr Cys Asn Gly Glu Ser Tyr Arg Gly Leu Met
            180             185             190

Asp His Thr Glu Ser Gly Lys Ile Cys Gln Arg Trp Asp His Gln Thr
    195             200             205

Pro His Arg His Lys Phe Leu Pro Glu Arg Tyr Pro Asp Lys Gly Phe
    210             215             220

Asp Asp Asn Tyr Cys Arg Asn Pro Asp Gly Gln Pro Arg Pro Trp Cys
225             230             235             240

Tyr Thr Leu Asp Pro His Thr Arg Trp Glu Tyr Cys Ala Ile Lys Thr
            245             250             255

Cys Ala Asp Asn Thr Met Asn Asp Thr Asp Val Pro Leu Glu Thr Thr
            260             265             270

Glu Cys Ile Gln Gly Gln Gly Glu Gly Tyr Arg Gly Thr Val Asn Thr
    275             280             285

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Ile Trp Asn Gly Ile Pro Cys Gln Arg Trp Asp Ser Gln Tyr Pro His
    290                 295                 300

Glu His Asp Met Thr Pro Glu Asn Phe Lys Cys Lys Asp Leu Arg Glu
305                 310                 315                     320

Asn Tyr Cys Arg Asn Pro Asp Gly Ser Glu Ser Pro Trp Cys Phe Thr
                325                 330                 335

Thr Asp Pro Asn Ile Arg Val Gly Tyr Cys Ser Gln Ile Pro Asn Cys
            340                 345                 350

Asp Met Ser His Gly Gln Asp Cys Tyr Arg Gly Asn Gly Lys Asn Tyr
        355                 360                 365

Met Gly Asn Leu Ser Gln Thr Arg Ser Gly Leu Thr Cys Ser Met Trp
    370                 375                 380

Asp Lys Asn Met Glu Asp Leu His Arg His Ile Phe Trp Glu Pro Asp
385                 390                 395                     400

Ala Ser Lys Leu Asn Glu Asn Tyr Cys Arg Asn Pro Asp Asp Asp Ala
                405                 410                 415

His Gly Pro Trp Cys Tyr Thr Gly Asn Pro Leu Ile Pro Trp Asp Tyr
            420                 425                 430

Cys Pro Ile Ser Arg Cys Glu Gly Asp Thr Thr Pro Thr Ile Val Asn
        435                 440                 445

Leu Asp His Pro Val Ile Ser Cys Ala Lys Thr Lys Gln Leu Arg
    450                 455                 460
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Met Ser Arg Lys Arg Arg Asn Thr Ile His Glu Phe Lys Lys Ser Ala
1               5               10              15

aag act acc cta atc aaa ata gat cca gca ctg aag ata aaa acc aaa         96
Lys Thr Thr Leu Ile Lys Ile Asp Pro Ala Leu Lys Ile Lys Thr Lys
            20              25              30

aaa gtg aat act gca gac caa tgt gct aat aga tgt act agg aat aaa        144
Lys Val Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn Lys
        35              40              45

gga ctt cca ttc act tgc aag gct ttt gtt ttt gat aaa gca aga aaa       192
Gly Leu Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg Lys
    50              55              60

caa tgc ctc tgg ttc ccc ttc aat agc atg tca agt gga gtg aaa aaa       240
Gln Cys Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys Lys
65              70              75              80

gaa ttt ggc cat gaa ttt gac ctc tat gaa aac aaa gac tac att aga       288
Glu Phe Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile Arg
            85              90              95

aac tgc atc att ggt aaa gga cgc agc tac aag gga aca gta tct atc       336
Asn Cys Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser Ile
            100             105             110

act aag agt ggc atc aaa tgt cag ccc tgg agt tcc atg ata cca cac       384
Thr Lys Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro His
            115             120             125

gaa cac agc ttt ttg cct tcg agc tat cgg ggt aaa gac cta cag gaa       432
Glu His Ser Phe Leu Pro Ser Ser Tyr Arg Gly Lys Asp Leu Gln Glu
    130             135             140

aac tac tgt cga aat cct cga ggg gaa gaa ggg gga ccc tgg tgt ttc       480
Asn Tyr Cys Arg Asn Pro Arg Gly Glu Glu Gly Gly Pro Trp Cys Phe
145             150             155             160

aca agc aat cca gag gta cgc tac gaa gtc tgt gac att cct cag tgt       528
Thr Ser Asn Pro Glu Val Arg Tyr Glu Val Cys Asp Ile Pro Gln Cys
            165             170             175

tca gaa gtt gaa tgc atg acc tgc aat ggg gag agt tat cga ggt ctc       576
Ser Glu Val Glu Cys Met Thr Cys Asn Gly Glu Ser Tyr Arg Gly Leu
            180             185             190

atg gat cat aca gaa tca ggc aag att tgt cag cgc tgg gat cat cag       624
Met Asp His Thr Glu Ser Gly Lys Ile Cys Gln Arg Trp Asp His Gln
            195             200             205
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- 7 -

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aca cca cac cgg cac aaa ttc ttg cct gaa aga tat ccc gac aag ggc    672
Thr Pro His Arg His Lys Phe Leu Pro Glu Arg Tyr Pro Asp Lys Gly
    210             215             220

ttt gat gat aat tat tgc cgc aat ccc gat ggc cag ccg agg cca tgg    720
Phe Asp Asp Asn Tyr Cys Arg Asn Pro Asp Gly Gln Pro Arg Pro Trp
225             230             235             240

tgc tat act ctt gac cct cac acc cgc tgg gag tac tgt gca att aaa    768
Cys Tyr Thr Leu Asp Pro His Thr Arg Trp Glu Tyr Cys Ala Ile Lys
            245             250             255

aca tgc gct gac aat act atg aat gac act gat gtt cct ttg gaa aca    816
Thr Cys Ala Asp Asn Thr Met Asn Asp Thr Asp Val Pro Leu Glu Thr
            260             265             270

act gaa tgc atc caa ggt caa gga gaa ggc tac agg ggc act gtc aat    864
Thr Glu Cys Ile Gln Gly Gln Gly Glu Gly Tyr Arg Gly Thr Val Asn
            275             280             285

acc att tgg aat gga att cca tgt cag cgt tgg gat tct cag tat cct    912
Thr Ile Trp Asn Gly Ile Pro Cys Gln Arg Trp Asp Ser Gln Tyr Pro
    290             295             300

cac gag cat gac atg act cct gaa aat ttc aag tgc aag gac cta cga    960
His Glu His Asp Met Thr Pro Glu Asn Phe Lys Cys Lys Asp Leu Arg
305             310             315             320

gaa aat tac tgc cga aat cca gat ggg tct gaa tca ccc tgg tgt ttt   1008
Glu Asn Tyr Cys Arg Asn Pro Asp Gly Ser Glu Ser Pro Trp Cys Phe
            325             330             335

acc act gat cca aac atc cga gtt ggc tac tgc tcc caa att cca aac   1056
Thr Thr Asp Pro Asn Ile Arg Val Gly Tyr Cys Ser Gln Ile Pro Asn
            340             345             350

tgt gat atg tca cat gga caa gat tgt tat cgt ggg aat ggc aaa aat   1104
Cys Asp Met Ser His Gly Gln Asp Cys Tyr Arg Gly Asn Gly Lys Asn
            355             360             365

tat atg ggc aac tta tcc caa aca aga tct gga cta aca tgt tca atg   1152
Tyr Met Gly Asn Leu Ser Gln Thr Arg Ser Gly Leu Thr Cys Ser Met
    370             375             380

tgg gac aag aac atg gaa gac tta cat cgt cat atc ttc tgg gaa cca   1200
Trp Asp Lys Asn Met Glu Asp Leu His Arg His Ile Phe Trp Glu Pro
385             390             395             400

gat gca agt aag ctg aat gag aat tac tgc cga aat cca gat gat gat   1248
Asp Ala Ser Lys Leu Asn Glu Asn Tyr Cys Arg Asn Pro Asp Asp Asp
            405             410             415

gct cat gga ccc tgg tgc tac acg gga aat cca ctc att cct tgg gat   1296
Ala His Gly Pro Trp Cys Tyr Thr Gly Asn Pro Leu Ile Pro Trp Asp
            420             425             430
```

```
tat tgc cct att tct cgt tgt gaa ggt gat acc aca cct aca atc gtt      1344
Tyr Cys Pro Ile Ser Arg Cys Glu Gly Asp Thr Thr Pro Thr Ile Val
        435                 440                 445
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taa tag
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            20                  25                  30
```

```
Lys Val Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn Lys
            35                  40                  45
```

```
Gly Leu Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg Lys
        50                  55                  60
```

```
Gln Cys Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys Lys
65                  70                  75                  80
```

```
Glu Phe Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile Arg
                85                  90                  95
```

```
Asn Cys Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser Ile
            100                 105                 110
```

```
Thr Lys Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro His
            115                 120                 125
```

```
Glu His Ser Phe Leu Pro Ser Ser Tyr Arg Gly Lys Asp Leu Gln Glu
        130                 135                 140
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```
Asn Tyr Cys Arg Asn Pro Arg Gly Glu Glu Gly Gly Pro Trp Cys Phe
145             150             155             160

Thr Ser Asn Pro Glu Val Arg Tyr Glu Val Cys Asp Ile Pro Gln Cys
                165             170             175

Ser Glu Val Glu Cys Met Thr Cys Asn Gly Glu Ser Tyr Arg Gly Leu
            180             185             190

Met Asp His Thr Glu Ser Gly Lys Ile Cys Gln Arg Trp Asp His Gln
        195             200             205

Thr Pro His Arg His Lys Phe Leu Pro Glu Arg Tyr Pro Asp Lys Gly
    210             215             220

Phe Asp Asp Asn Tyr Cys Arg Asn Pro Asp Gly Gln Pro Arg Pro Trp
225             230             235             240

Cys Tyr Thr Leu Asp Pro His Thr Arg Trp Glu Tyr Cys Ala Ile Lys
            245             250             255

Thr Cys Ala Asp Asn Thr Met Asn Asp Thr Asp Val Pro Leu Glu Thr
            260             265             270

Thr Glu Cys Ile Gln Gly Gln Gly Glu Gly Tyr Arg Gly Thr Val Asn
        275             280             285

Thr Ile Trp Asn Gly Ile Pro Cys Gln Arg Trp Asp Ser Gln Tyr Pro
    290             295             300

His Glu His Asp Met Thr Pro Glu Asn Phe Lys Cys Lys Asp Leu Arg
305             310             315             320

Glu Asn Tyr Cys Arg Asn Pro Asp Gly Ser Glu Ser Pro Trp Cys Phe
            325             330             335

Thr Thr Asp Pro Asn Ile Arg Val Gly Tyr Cys Ser Gln Ile Pro Asn
            340             345             350

Cys Asp Met Ser His Gly Gln Asp Cys Tyr Arg Gly Asn Gly Lys Asn
        355             360             365

Tyr Met Gly Asn Leu Ser Gln Thr Arg Ser Gly Leu Thr Cys Ser Met
370             375             380
```

Trp Asp Lys Asn Met Glu Asp Leu His Arg His Ile Phe Trp Glu Pro
385                 390             395                 400

Asp Ala Ser Lys Leu Asn Glu Asn Tyr Cys Arg Asn Pro Asp Asp Asp
                405                 410                 415

Ala His Gly Pro Trp Cys Tyr Thr Gly Asn Pro Leu Ile Pro Trp Asp
                420                 425                 430

Tyr Cys Pro Ile Ser Arg Cys Glu Gly Asp Thr Thr Pro Thr Ile Val
                435                 440                 445